42. The method of claim 1, wherein the effective amount of the β_2 adrenergic agonist is from about 10 to about 100 μg per kg of body weight.

43. The method of claim 1, wherein the effective amount of the β_2 adrenergic agonist is about 40 μg per kg of body weight.

Remarks

Claims 1-36 were pending at the time of examination. Of those claims, claims 1-10 were drawn to an elected restriction group, and claims 1, 4, 6, 7 and 9 were drawn to the elected species of β_2 adrenergic agonist, clenbuterol. With this amendment, claims 11-20 and 32-36 are cancelled, claims 1, 4, 5, 6, 7, 8, 9 and 10 are amended, and claims 37-43 are added to more particularly point out and distinctly claim the invention.

The claim amendments and additions are supported in the specification as filed as follows:

Support for the dosages recited in amended claims 1, 6, 7 and 8, and new claims 42 and 43 is found in the specification at least at page 9, lines 1-8.

Support for "contusion" is found at least at page 9, lines 14-21, where a contusion injury was used as the experimental model in the Experimental Methods section.

Support for the recitation of "lower thoracic spine" in claim 37 is based at least on the Experimental Methods, at page 9, lines 14-21, where a contusion injury at the T10 vertebra was imposed on the experimental animals. T10 is well known to the skilled artisan as being part of the lower thoracic vertebrae, which consist of T10-T12. For supporting literature for this, see page 1 of "Thoracic Screw Placement in Deformity: Technique Pitfalls, Complications, Results" found at http://www.spineuniverse.com/1p/srs/imast/lenkeimast.html, copy enclosed herewith.

Rejection under 35 U.S.C. 112, first paragraph

Claim 9 stands rejected under 35 U.S.C. 112, first paragraph as not being described in the specification as filed. Specifically, the dosage recitation of 0.25 g/kg/day is deemed to not be supported in the specification. Reconsideration and withdrawal of this rejection is requested in light of the amendment to claim 9 and the following discussion.

Claim 9 has been amended to depend from claim 40, and to recite 0.25 mg/kg/day, which is supported in the specification at page 17, lines 10-19. Accordingly, applicants request withdrawal of the written description rejection under 35 U.S.C. 112, first paragraph.

Rejections under 35 U.S.C. 102(a)

Claims 1 and 4 stand rejected under 35 U.S. C. 102(a) as being anticipated by Zeman et al. (Exper. Neurol. 1999, 159:267-273). Applicants request reconsideration and withdrawal of this rejection because the reference is applicants' own work.

Rejections under 35 U.S.C. 102(b)

Claims 1, 4, 6 and 7 stand rejected under 35 U.S.C. 102(b) as being anticipated by Etlinger et al., WO99/09956. It is argued that the claimed method is inherent in the method of treatment of scoliosis disclosed in the cited reference. Applicants respectfully request reconsideration and withdrawal of these rejections based on the claim amendments and the following discussion.

All of the rejected claims as amended recite methods of rehabilitation of a mammalian patient with a spinal cord contusion injury or motor neuron degeneration. However, Etlinger et al. does not disclose the treatment of any mammalian patient with

a spinal cord contusion injury or motor neuron degeneration. Applicants note that the injury induced in the Experimental Methods of Etlinger et al. was a severing of three-quarters of the spinal cord. See Etlinger et al., page 11, lines 28-31. Also, the discussion of what is known about scoliosis in Etlinger et al., at page 7, lines 18-26, indicates that the condition is caused by systemic neuromuscular disease such as muscular dystrophy or an injury that causes a weakening of the muscles supporting one side of the spine, such as the severing injury induced in those studies, but not a contusion injury or motor neuron degeneration as in the instant claims. Therefore, Etlinger et al. does not disclose administering a β_2 adrenergic agonist to a mammalian patient with spinal cord contusion injury or motor neuron degradation as required in the rejected claims. Accordingly, applicants respectfully request withdrawal of the rejections under 35 U.S.C. 102(b) based on Etlinger et al.

Claims 1, 4, 6 and 7 also stand rejected under 35 U.S.C. 102(b) as being anticipated by Sayers et al., Soc. Neuroscience Abstracts 1998; 24: abstract 125.2. It is argued that Sayers et al. anticipates the rejected claims because that reference teaches the use of 1 mg/kg/day of clenbuterol in treating a spinal cord injury. Applicants respectfully request reconsideration and withdrawal of these rejections based on the claim amendments and the following discussion.

Applicants note that amended claim 1 recites treatment with an effective dose of at least one β_2 adrenergic agonist of about 0.5 to about 100 μg (i.e., 0.0005 to 0.1 mg) per kg body weight per day. This is a considerably lower dose than the effective dose disclosed in Sayers et al. It is also noted that Sayers et al. discloses that 10 μg/kg/day was ineffective in improving behavioral recovery. Therefore, Sayers et al. does not disclose the method claimed in amended claim 1. Additionally, the skilled artisan would have had strong doubt at the time of filing that the claimed method would be effective in

causing reduction of locomotor function and neuromuscular strength because Sayers et al. discloses that a dosage of 10 μg/ml of clenbuterol is ineffective.

Amended claims 4, 6 and 7 depend from claim 37, and thus requires that the treatment be for a contusion injury to the lower thoracic vertebrae, or T10-T12. Since Sayers et al. only discloses treatment of a contusion injury at the T8 level, it does not disclose the methods claimed in claims 4, 6 or 7. Applicants therefore respectfully request withdrawal of the rejection of claims 4, 6 and 7 under 35 U.S.C. 102(b) as being anticipated by Sayers et al.

Conclusion

In light of the claim amendments and the above discussion, applicants respectfully request withdrawal of all current rejections and the search and examination of the claims encompassing the nonelected species. If there are any minor issues preventing this, applicants urge that the examiner contact the undersigned attorney.

Respectfully submitted,

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Dated: New York, New York
March 25, 2002

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Marked up Examined Claims - U.S. Patent Application 09/611,662
Deletions are bracketed and additions are underlined

1. A method of rehabilitation following spinal cord contusion injury or motor neuron degeneration, the method comprising administering to a mammalian patient with spinal cord contusion injury [to the spinal cord]or motor neuron degeneration causing reduction of locomotor function and neuromuscular strength, a therapeutically effective amount of at least one β_2 adrenergic agonist to increase locomotor function and neuromuscular strength in the patient, wherein the effective amount of the β_2 adrenergic agonist is from about 0.5 to about 100 μg per kg of body weight.

4. The method of claim 1, wherein the β_2 adrenergic agonist comprises clenbuterol [and salts]or a salt thereof.

5. The method of claim 1 wherein the β_2 adrenergic agonist comprises salbutamol [and salts]or a salt thereof.

6. The method of claim [1]37 wherein the effective amount of the β_2 adrenergic agonist is from about 0.5 to about 1000 μg per kg of body weight.

7. The method of claim [4]40 wherein the effective amount of clenbuterol is from about 0.5 to about 1000 μg per kg of body weight.

8. The method of claim [5]41 wherein the effective amount of salbutamol is from about 0.5 to about 1000 μg per kg of body weight.

9. The method of claim [4]40, wherein the effective amount of clenbuterol is greater than about 0.25 mg/day per kg body weight.

10. The method of claim [5]41, wherein the effective amount of salbutamol is greater than about 0.25 mg/day per kg body weight.

Thoracic Screw Placement in Deformity: Technique Pitfalls, Complications, Results

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I. Technique - Free Hand Placement of Thoracic Pedicle Screws

1. Meticulous exposure - all bony landmarks exposed:
   pars
   facet
   t.p. - out to tip

2.Begin most caudal level (neutral rotation and largest pedicle) - remember that LI and L2 pedicles are smaller diameter than TIO-TI2!

3.Starting point (mark with drill bit)

lower thoracic (TIO-TI2) - down slope of bisected t.p. at junction of t.p. and lamina at same level as lateral pars

mid-thoracic (T4-T9) -junction of down slope of proximal t.p. and lamina at base of superior facet, medical to lateral pars

proximal thoracic (T I -T3) -junction of proximal t.p. and lamina medial to lateral pars

4.Burr small (~ 5 mm) defect in dorsal cortex and search for "pedicle blush" of bleeding cancellous bone that indicates entrance to pedicle

may not be seen in very small apical thoracic pedicles

5.Blunt slightly curved gear shift used with ~ 2 mm rounded tip:

Orientation -

frontal: perpendicular to lamina (superior facet)

sagittal: cephalad (lower thoracic) orientation versus caudad (upper thoracic) orientation

axial: based on degree of rotational deformity obviously maximal at apex of scoliosis

6.Advanced gear shift first pointing slightly lateral and then once engaged at base of pedicle, turn tip 180° to point slightly medial to advance down pedicle into the vertebral body

7.Should advance smoothly and snug without any jump/catches. If in doubt, head more lateral! Okay to poke out lateral, no structures at risk (first 1-2 cm), than this provides orientation to more medial pedicle.

8. Probe advancement should be snug, if loose - probably out lateral. If cannot advance, probably aiming too medial!

9. Palpate five walls of pathway:

- bony floor (vertebral body) and four pedicle walls (medial, lateral, superior, inferior)

10.If completely interosseous, place TAP/smaller screw (.5 mm) less diameter than anticipated